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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,545	12/18/2006	Berislav V. Zlokovic	GRT/5192-16	4761
23117 7590 03/12/2008 NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203				
EXAMINER				
CHANDRA, GYAN				
ART UNIT		PAPER NUMBER		
1646				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/537,545

**Applicant(s)**

ZLOKOVIC ET AL.

**Examiner**

GYAN CHANDRA

**Art Unit**

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**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 8-22, 24, 25 and 27-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 8-22, 24, 25 and 27-32 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SI/08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

## DETAILED ACTION

### *Election/Restrictions*

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 8-11, drawn to a composition comprising an activated protein C, a prodrug or functional variant thereof.

Group 2, claim(s) 12-20, and 29-32 drawn to a method of treating cell stress or injury comprising administering an effective amount of an activated protein C, a prodrug or functional variant thereof to a human subject.

Group 3, claim(s) 21-22, drawn to a method of reducing p53 signaling in at least one cell type of a subject by an activated protein C, a prodrug or functional variant thereof.

Group 4, claim(s) 24, drawn to a method of screening for an agent comprising providing a library of candidate agents which are variants for activate protein C and/or protein C, determining p53 signaling activity in the presence of a candidate agent and selecting an agent which inhibits p53 signaling activity.

Group 5, claim(s) 25, drawn to a method of screening for an agent comprising providing a library of candidate agents which are variants for activate protein C and/or protein C, determining activity of one or more receptors selected from the group consisting of PAR-1, PAR-3 and EPCR and selecting an agent which is an agonist of PAR-1 and/or PAR-3 and/or EPCR.

Group 6, claim(s) 27, as drawn to a method of neuroprotection in a subject in need of treatment by an agonist of PAR-1.

Group 7, claim(s) 27, as drawn to a method of neuroprotection in a subject in need of treatment by an agonist of PAR-3.

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Group 8, claim(s) 27, as drawn to a method of neuroprotection in a subject in need of treatment by an agonist of EPCR.

Group 9, claim(s) 27, as drawn to a method of neuroprotection in a subject in need of treatment by an agonist of PAR-1 and PAR-3.

Group 10, claim(s) 27, as drawn to a method of neuroprotection in a subject in need of treatment by an agonist of PAR-1 and EPCR.

Group 11, claim(s) 27, as drawn to a method of neuroprotection in a subject in need of treatment by an agonist of PAR-3 and EPCR.

Group 12, claim(s) 27, as drawn to a method of neuroprotection in a subject in need of treatment by an agonist of PAR-1, PAR-3 and EPCR.

Group 13, claim(s) 27-28, as drawn to a method of neuroprotection in a subject in need of treatment by a TFLLRNPNDK peptide.

The inventions listed as Groups 1-13 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group 1 is anticipated by Griffin et al. (US Pub. No. 2002/0028199, Published on March 07, 2002) Griffin et al teach the special technical features of a composition comprising APC and a method of treating a subject in need thereof using said composition (see page 4, right column, page 5, page 6 right column and pages 7-8). Therefore, Group 1 lacks a special technical feature and cannot share one with the other inventions of Groups 2-13.

Group 2, recites the special technical feature of treating cell stress or injury comprising administering an effective amount of an activated protein C, a prodrug or functional variant thereof to a human subject, which is not required by the methods of Groups 3-13.

Group 3, recites the special technical feature of reducing p53 signaling in at least one cell type of a subject by an activated protein C, a prodrug or functional variant thereof, which is not required by the methods of Groups 2 and 4-13.

Group 4, recites the special technical feature of screening for an agent comprising providing a library of candidate agents which are variants for activate protein C and/or protein C, determining p53 signaling activity in the presence of a candidate agent and selecting an agent which inhibits p53 signaling activity, which is not required by the methods of Groups 2-3 and 5-13.

Group 5, recites the special technical feature of screening for an agent comprising providing a library of candidate agents which are variants for activate protein C and/or

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protein C, determining activity of one or more receptors selected from the group consisting of PAR-1, PAR-3 and EPCR and selecting an agent which is an agonist of PAR-1 and/or PAR-3 and/or EPCR, which is not required by the methods of Groups 2-4 and 6-13.

Group 6, recites the special technical feature of neuroprotection in a subject in need of treatment by an agonist of PAR-1, which is not required by the methods of Groups 2-5 and 7-13.

Group 7, recites the special technical feature of neuroprotection in a subject in need of treatment by an agonist of PAR-3, which is not required by the methods of Groups 2-6 and 8-13.

Group 8, recites the special technical feature of neuroprotection in a subject in need of treatment by an agonist of EPCR, which is not required by the methods of Groups 2-7 and 9-13.

Group 9, recites the special technical feature of neuroprotection in a subject in need of treatment by an agonist of PAR-1 and PAR-3, which is not required by the methods of Groups 2-8 and 10-13.

Group 10, recites the special technical feature of neuroprotection in a subject in need of treatment by an agonist of PAR-1 and EPCR, which is not required by the methods of Groups 2-9 and 11-13.

Group 11, recites the special technical feature of neuroprotection in a subject in need of treatment by an agonist of PAR-3 and EPCR, which is not required by the methods of Groups 2-10 and 12-13.

Group 12, recites the special technical feature of neuroprotection in a subject in need of treatment by an agonist of PAR-1, PAR-3 and EPCR, which is not required by the methods of Groups 2-11 and 13.

Group 13, recites the special technical feature of neuroprotection in a subject in need of treatment by a TFLLRNPNDK peptide, which is not required by the methods of Groups 2-12.

The examiner has required restriction between product and process claims.

Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or

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otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01

#### Further Restriction

##### Group 2

If Group 2 is elected, a further restriction to one of the following inventions is

required under 35 U.S.C. 121 or 372:

Activated protein C mutants: The inventions of Group 2 are drawn to the special technical features of different activate protein C mutants (i.e., K191A, K192A, K193A, R229A and R230A).

Each of the claimed mutants are different amino acid mutations. Each mutation in context to the protein would result in functionally and structurally distinct molecules. Therefore, Applicant must choose 1 activated protein mutant against which the search should be performed.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

**Neurodegenerative disease:** The invention is drawn to a number of patentably distinct neurodegenerative diseases listed in claim 31 (i.e., Alzheimer's disease, Down syndrome, Huntington's disease and Parkinson's disease).

The species are independent or distinct because claims to the different species recite the mutually exclusive characteristics of such species and that each species is different from other species in its structure and function relationship such as Parkinson's disease is very different than Down syndrome or Huntington's disease. In addition, these species are not obvious variants of each other based on the current record.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would

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not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

- (a) the inventions have acquired a separate status in the art in view of their different classification;
- (b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
- (c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);
- (d) the prior art applicable to one invention would not likely be applicable to another invention;



(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

**Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention and (ii) the species to be examined even though the requirement may be traversed (37 CFR 1.143) and (iii) identification of the claims encompassing the elected invention and the elected species.**

The election of an invention and the species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention and species.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions or the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions or the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

**If applicant elects Group 2, a single activated protein C and one species from the neurodegenerative disease group must be elected to be considered fully responsive. It noted that the election of a mutant is restriction election and a species election.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gyan Chandra  
Art Unit 1646  
22 February 2008  
Fax: 571-273-2922

/Robert Landsman/  
Primary Examiner, Art Unit 1647